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ORIGINAL ARTICLE



# Evidence-based proposal for the number of ambulatory readings required for assessing blood pressure level in research settings: an analysis of the IDACO database

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## ABSTRACT

**Background:** Guidelines on the required number of ambulatory blood pressure (ABP) readings focus on individual patients. Clinical researchers often face the dilemma of applying recommendations and discarding potentially valuable information or accepting fewer readings.

**Methods:** Starting from ABP recordings with ≥30/≥10 awake/asleep readings in 4277 participants enrolled in eight population studies in the International Database on Ambulatory Blood Pressure in Relation to Cardiovascular Outcomes (IDACO), we randomly selected a certain number of readings (from 30 to 1 awake and 10 to 1 asleep readings) at a time over 1000 bootstraps at each step. We evaluated: (i) concordance of the ABP level; (ii) consistency of the cross-classification based on office blood pressure and ABP; and (iii) accuracy in predicting cardiovascular complications. For each criterion, we fitted a regression line joining data points relating outcome to the number of readings covering the ranges of 30-20/10-7 for awake/asleep readings.

**Results:** Reducing readings widened the SD of the systolic/diastolic differences between full (reference) and selected recordings from 1.7/1.2 (30 readings) to 14.3/10.3 mm Hg (single reading) during wakefulness, and from 1.9/1.4 to 10.3/7.7 mm Hg during sleep; lowered the κ statistic from 0.94 to 0.63, and decreased the hazard ratio associated with 10/5 mm Hg increments in systolic/diastolic ABP from 1.21/1.14 to 1.06/1.04 during wakefulness and from 1.26/1.17 to 1.14/1.08 during sleep. The first data points falling off these regression lines during wakefulness/sleep corresponded to 8/3 and 8/4 readings for criteria (i) and (iii) and to 5 awake readings for criterion (ii).

**Conclusions:** 24-h ambulatory recordings with ≥8/≥4 awake/asleep readings yielded ABP levels similar to recordings including the guideline-recommended ≥20/≥7 readings. These criteria save valuable data in a research setting, but are not applicable to clinical practice.

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## Introduction

The Global Burden of Diseases Study 2010 reported that high blood pressure is the leading risk factor for ill health and causes 9.4 million deaths every year — more than half of the estimated 17 million deaths per year attributable to total cardiovascular disease [1,2]. North American [3,4], European [5,6] Japanese [7] and Chinese [8] guidelines unanimously recommend ambulatory blood pressure monitoring as the state-of-the-art technology to be used. Wearing an ambulatory blood pressure monitor causes discomfort that increases with the number of cuff inflations during normal daily activities and sleep. Current recommendations on the number of ambulatory readings required for estimating the 24-h, awake or asleep blood pressure levels are focusing on the management of hypertension in individual patients. Recommendations vary from obtaining at least 70% of the programmed readings without providing a specific number [6,9] to 20 awake or daytime and 7 asleep or nighttime readings [6].

For analysis of the International Database on Ambulatory Blood Pressure in Relation to Cardiovascular Outcomes (IDACO) [10–12], we consistently applied short fixed clock time interval excluding the transition periods in the morning and evening, when in most people blood pressure level rapidly changes upon awaking or going to sleep, and we set the standard to 10 daytime and 5 nighttime readings [10–12]. We re-analyzed the IDACO database with as objective to determine how many readings are required to capture the awake and asleep blood pressure in epidemiological studies. While using full recordings as the reference, we applied three criteria: (i) concordance of the blood pressure level between full and randomly reduced recordings; (ii) consistency of the cross-classification based on office and the awake blood pressure; and (iii) maintenance of the accuracy in predicting cardiovascular complications.

## Methods

### Study population

Previous publications have described the IDACO database in detail [10–12]. Population studies qualified for inclusion if information on the office and the ambulatory blood pressure and cardiovascular risk factors was available at baseline and if follow-up included both fatal and nonfatal outcomes. All studies received ethical approval and adhered to the principles of the Declaration of Helsinki [13]. Participants gave written informed consent. Of the 13,111 people included in the database, we selected 4277 [14–20] based on the following criteria: (i) availability of a diary; and (ii) at least 30 readings during wakefulness and 10 readings during sleep.

### Blood pressure measurement

The office blood pressure was the average of two readings. We programmed blood pressure monitors to obtain ambulatory readings at 30-minute intervals throughout the whole day [18], or at intervals ranging from 15 [16,17,20] to 20 [14,15,19] minutes during wakefulness and at intervals of 30 [16,17,20], 40 [14,15] or 45 [19] minutes during sleep. The same SAS macro processed all ambulatory recordings, which remained unedited or were sparsely edited [18]. For the main analysis, we determined the awake and asleep periods from the participants' diary cards. We applied guideline-endorsed criteria [3–8] to define office and ambulatory hypertension and to categorize individuals based on office and awake ambulatory blood pressure into normotensive people and patients with white-coat, masked and sustained hypertension, irrespective of antihypertensive drug treatment [21]. If systolic and diastolic blood pressure fell in different categories, participants were assigned to the highest category. In sensitivity analyses, we defined daytime as the interval from 10 AM to 8 PM in Europeans [14,16,17,20] and South Americans [15] and from 8 AM to 6 PM in Asians [18,19]. The corresponding nighttime intervals ranged from midnight to 6 AM [14–17,20] and from 10 PM to 4 AM [18,19], respectively. These fixed intervals eliminate the transition periods in the morning and evening when blood pressure changes rapidly, resulting in daytime and nighttime blood pressure levels that are within 1–2 mm Hg of the awake and asleep levels [22].

### Ascertainment of events

We ascertained vital status and the incidence of fatal and nonfatal illnesses from the appropriate sources in each country. Outcomes were coded according to the international classification of diseases (ICD). The cardiovascular endpoint included cardiovascular mortality, sudden death, heart failure and other nonfatal cardiac, coronary and cerebrovascular complications, not including transient ischemic attack.

### Statistical analysis

For database management and statistical analysis, we used SAS software version 9.4 (SAS Institute

Inc., Cary, NC). Significance was a two-tailed α-level of 0.05 or less. Means and proportions were compared using a large sample z-test and Fisher's exact test, respectively.

Starting from full recordings, we applied the PROC SURVEYSELECT procedure as implemented in the SAS package to select in a random manner awake and asleep readings without replacement. While using full recordings as the reference, we determined the minimum number of awake and asleep readings required to satisfy three criteria: (i) concordance of the blood pressure level between full and reduced recordings; (ii) consistency of the cross-classification based on office and the ambulatory blood pressure; and (iii) maintenance of the accuracy in predicting cardiovascular complications. We bootstrapped all analyses at each step of data reduction to obtain the mean of 1000 point estimates for each criterion. We assessed the concordance of the blood pressure level between full and reduced recordings from the SD of the mean differences between full and randomly reduced recordings. We applied the κ statistic for the assessment of the consistency of the classification of the awake and asleep blood pressure into normotension and ambulatory hypertension. Hypertension during wakefulness was a blood pressure of at least 135 mm Hg systolic or 85 mm Hg diastolic. 24-h ambulatory hypertension was a blood pressure of at least 130 mm Hg systolic or 80 mm Hg diastolic. The consistency of the prognostic value of the awake and asleep blood pressure was assessed from Cox models stratified for cohort and adjusted for sex, age, body mass index, office blood pressure, the total-to-high-density-lipoprotein cholesterol ratio, smoking and drinking, history of cardiovascular disease and diabetes mellitus, and antihypertensive treatment. We linearized the associations of the averages of the SDs (criterion i), κ statistics (criterion ii) or hazard ratios (criterion iii) with the number of readings retained in the recordings by a logarithmic transformation. After linearization of the association between the outcome criteria (SD, κ or hazard ratio) and the number of readings retained in the analysis, we drew a regression line through the data points derived from recordings with 30 awake and 10 asleep readings up to recordings including 20 awake and 7 asleep readings as recommended by the guidelines [6,9]. The first data point that fell off this regression line was used to determine the minimum required number of readings. By using this approach, we accounted for current guidelines [6,9]. We also estimated the number of readings required to estimate the ambulatory blood pressure level in individual subjects with a 5% precision compared with full recordings. A 5% precision was an absolute difference in the blood pressure level between reduced and full recordings within the 2.5 to 97.5th percentile interval of the signed differences.

## Results

### Baseline characteristics of participants

Of 4277 participants, 2233 (52.2%) were women, 3349 (78.3%) were White and 326 (7.6%) and 602 (14.1%) were Chinese and Japanese, respectively. Current smoking was reported by 1418 (33.2%) participants and drinking alcohol by 2530 (59.2%). The prevalence of diabetes was 237 (5.5%) and 324 participants (7.6%) had a history of cardiovascular disease. Age averaged 50.9 ± 14.7 years (5th–95th percentile interval, 24.1–71.9 years). Table 1 lists the baseline characteristics categorized by the incidence of cardiovascular events during follow-up. With the exception of drinking alcohol, cardiovascular risk factors had a higher prevalence or higher level in cases with incident cardiovascular complications compared with non-cases.

In all participants office systolic/diastolic blood pressure averaged 129.3/80.0 mm Hg. The median (5th to 95th percentile interval) number of ambulatory readings averaged to estimate the 24-h, awake, daytime, asleep and nighttime blood pressures were 73 (47–82), 56 (32–70), 37 (20–42), 15 (11–22) and 12 (8–13), respectively. Mean values of the 24-h, awake

**Table 1.** Baseline characteristics of participants by incident cardiovascular disease.

| Characteristic | Non-Cases | Cases | All |
|---|---|---|---|
| Number (%) of participants | 3660 | 617 | 4277 |
| Women | 1984 (54.2) | 249 (40.4) | 2233 (52.2) |
| Current smoking | 1177 (32.2) | 241 (39.1) | 1418 (33.2) |
| Drinking alcohol | 2164 (59.1) | 366 (59.3) | 2530 (59.2) |
| Diabetes | 171 (4.7) | 66 (10.7) | 237 (5.5) |
| Previous cardiovascular diseases | 200 (5.5) | 124 (20.1) | 324 (7.6) |
| White ethnicity | 2866 (78.4) | 481 (78.0) | 3349 (78.3) |
| Mean (±SD) characteristic | | | |
| Age, years | 48.9 ± 14.4 | 63.2 ± 10.2 | 50.9 ± 14.7 |
| Body mass index, kg/m$^2$ | 25.1 ± 4.2 | 26.0 ± 4.3 | 25.2 ± 4.3 |
| Total serum cholesterol, mmol/L | 5.52 ± 1.21 | 5.99 ± 1.19 | 5.59 ± 1.22 |
| HDL cholesterol, mmol/L | 1.39 ± 0.39 | 1.30 ± 0.39 | 1.37 ± 0.39 |
| Total-to-HDL cholesterol ratio | 4.32 ± 2.81 | 5.00 ± 2.12 | 4.42 ± 2.73 |
| Blood pressure, mm Hg | | | |
| Office systolic | 127.5 ± 18.3 | 140.0 ± 20.3 | 129.3 ± 19.1 |
| Office diastolic | 79.5 ± 11.2 | 83.0 ± 12.2 | 80.0 ± 11.5 |
| 24-h systolic | 122.4 ± 12.6 | 130.9 ± 14.5 | 123.7 ± 13.2 |
| 24-h diastolic | 73.3 ± 8.3 | 76.2 ± 8.9 | 73.7 ± 8.4 |
| Awake systolic | 128.1 ± 13.1 | 136.2 ± 15.0 | 129.3 ± 13.7 |
| Awake diastolic | 77.9 ± 8.6 | 80.3 ± 9.3 | 78.3 ± 8.7 |
| Asleep systolic | 110.5 ± 12.9 | 119.6 ± 15.7 | 111.8 ± 13.7 |
| Asleep diastolic | 63.8 ± 8.8 | 67.5 ± 9.5 | 64.3 ± 9.0 |

HDL indicates high-density lipoprotein. Differences between non-cases and cases were all significant ($p < .0001$) except for ethnicity and drinking alcohol ($p \geq .83$).

and asleep blood pressures in all participants were 123.7/73.7 mm Hg, 129.3/78.3 mm Hg and 111.8/64.3 mm Hg, respectively. The average daytime and nighttime blood pressures were all within 1.2 mm Hg systolic and 0.8 mm Hg diastolic of the corresponding diary-based awake and asleep levels.

### Criterion I: consistency of the ambulatory blood pressure level

Compared with full recordings, randomly reducing the number of readings to a single measurement over 1000 bootstraps did not yield mean differences in the blood pressure level at any bootstrap loop greater than 0.69 mm Hg systolic or 0.47 mm Hg diastolic during wakefulness or sleep (Figure 1), but widened the SD of the mean differences on average from 1.7 to 14.3 mm Hg systolic and from 1.2 to 10.3 mm Hg diastolic during wakefulness, and from 1.9 to 10.3 mm Hg systolic and from 1.4 to 7.7 mm Hg diastolic during sleep (Figure 2). Next, we linearized the vertical axes by a logarithmic transformation and fitted regression lines joining the data points from recordings with 30 awake and 10 asleep readings up to recordings including 20 awake and 7 asleep readings as recommended by the guidelines. For the awake and asleep blood pressures, the last data point still on the regression line was derived from recordings including 8 and 3 readings during wakefulness and sleep, respectively (Figure 2). Using a similar strategy, the number of daytime and nighttime readings was 6 and 3, respectively. In addition, based on individual blood pressure difference between reduced and full recordings, Table 2 provides the number of readings required to estimate blood pressure in individual subjects with a 5% precision.

### Criterion II: consistency of categorization

Of 4277 participants, 2371 (55.4%) were normotensive on office and awake ambulatory measurement, while 412 (9.6%), 538 (12.6%) and 956 (22.4%) had white-coat, masked or sustained hypertension. Using the 24-h ambulatory blood pressure instead of the blood pressure during wakefulness yielded similar numbers: 2430 (56.8%) for normotension and 444 (10.4%) 479 (11.2%) and 924 (21.6%) for white-coat, masked and sustained hypertension, respectively. Figure 3 shows the concordance in the discrimination between normotension and hypertension during wakefulness. The κ statistic was plotted over 1000 bootstraps randomly reduced recordings during

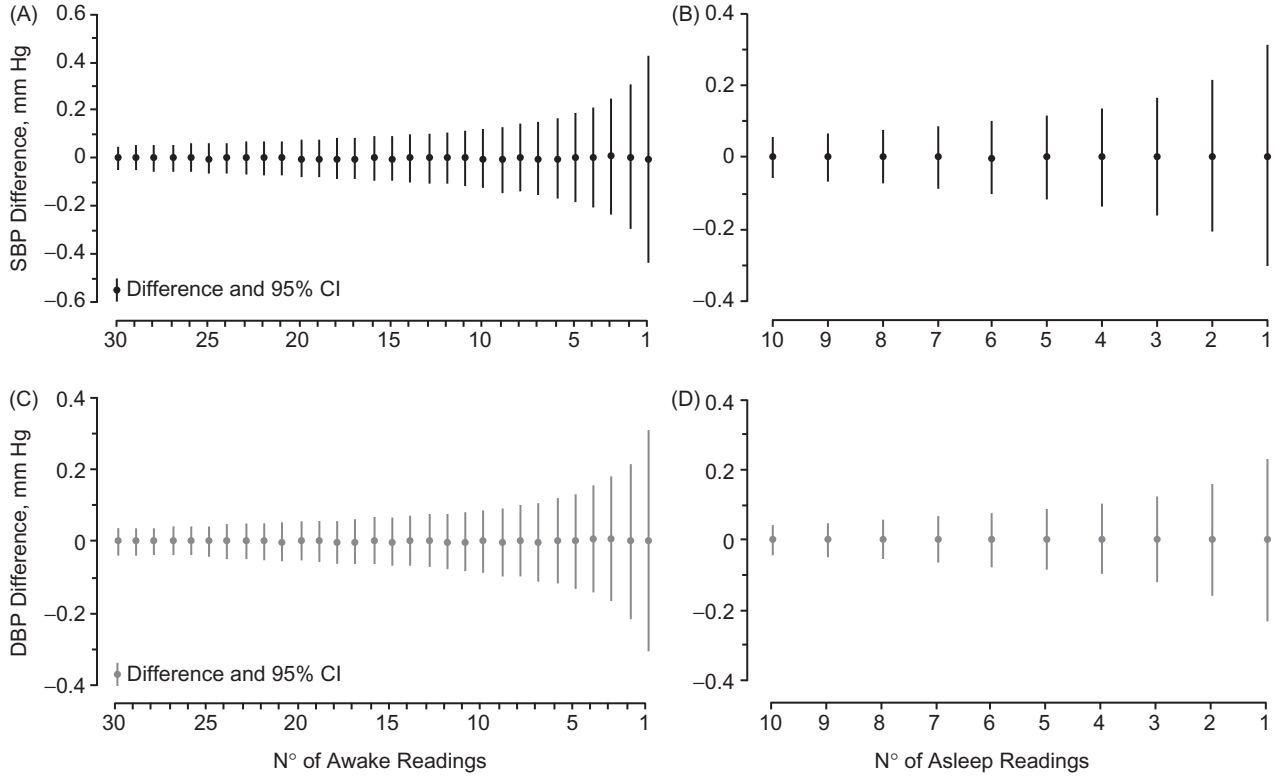


Figure 1. Differences between awake (A,C) and asleep (B,D) systolic (SBP) and diastolic (DBP) blood pressure levels derived from full recordings and randomly reduced recordings. Estimates at each step are means over 1000 bootstrap loops. Vertical bars denote the 95% confidence interval.

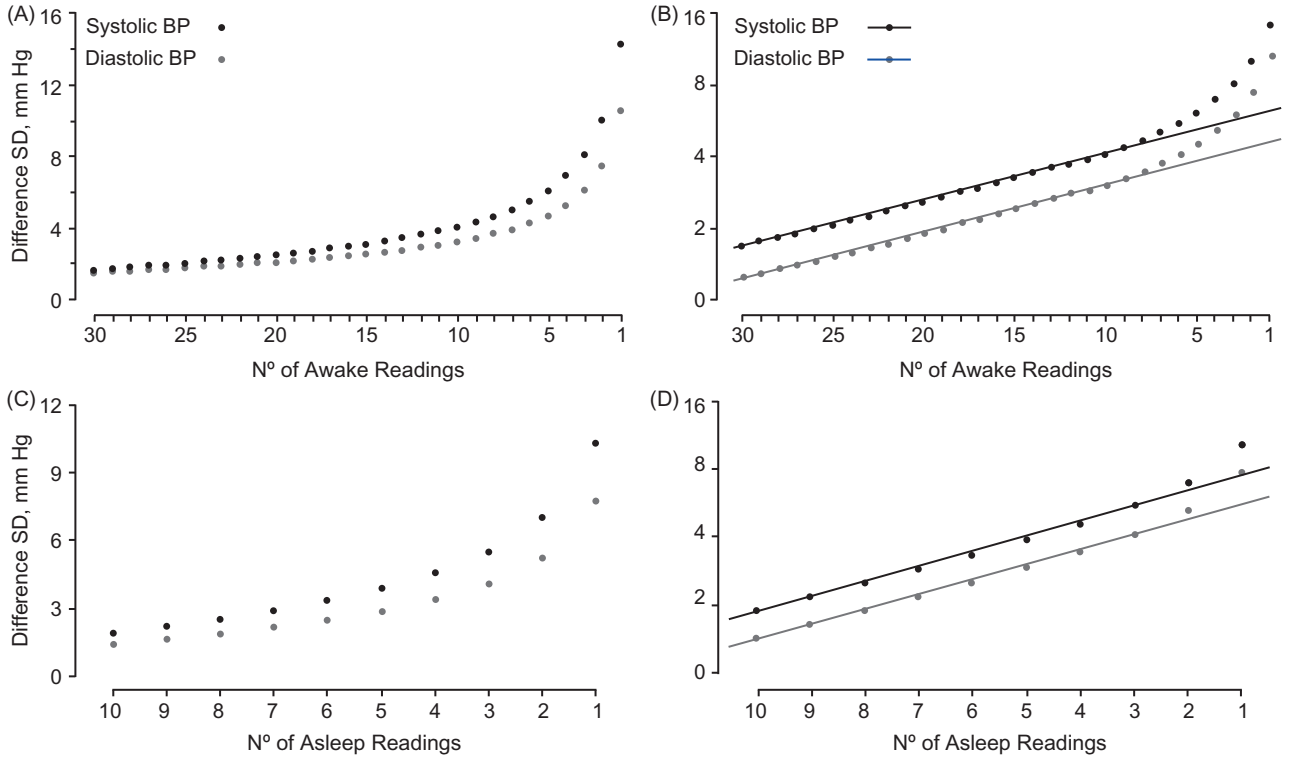


**Figure 2.** Standard deviation (SD) of the differences between awake (A) and asleep (C) systolic (SBP) and diastolic (DBP) blood pressures levels derived from full recordings and from over 1000 bootstraps randomly reduced recordings. After linearizing the vertical axis by a logarithmic transformation, regression lines were fitted joining the data points from recordings including 30 to 20 awake (B) and 10 to 7 asleep (D) readings. The last data point still on the regression line was derived from recordings including 8 and 3 readings during wakefulness and sleep, respectively.

wakefulness. After linearizing the horizontal axis by a logarithmic transformation, regression lines were fitted joining the data points from recordings including 30 to 20 awake readings. The last data point still on the regression line was for 5 readings. Using a similar strategy, the number of daytime readings required to correctly differentiate normotension from hypertension in daytime ambulatory readings was 3.

### *Criterion III: consistency of prediction of cardiovascular outcome*

Over a median follow-up of 14.4 years (5th–95th percentile interval, 2.4–24.4 years), 617 participants experienced a cardiovascular complication. The multivariable-adjusted hazard ratios associated with a 10/5 mm Hg higher systolic/diastolic blood pressure derived from full recordings were 1.21 (CI, 1.13 to 1.31) systolic and 1.14 (CI, 1.08 to 1.21) diastolic during wakefulness; the corresponding estimates were 1.28 (CI, 1.20 to 1.35) and 1.18 (CI, 1.12 to 1.24) for the period during sleep ($p < .0001$ for all). In fully reduced recordings with single reading, the mean hazard ratios of 1000 bootstraps decreased to 1.06 (CI, 1.02 to 1.11) systolic and 1.04 (CI, 1.01 to 1.07) diastolic during wakefulness and to 1.14 (CI, 1.09 to 1.19) systolic and 1.08 (CI, 1.04 to 1.12) diastolic during sleep.

Figure 4 depicts the multivariable-adjusted hazard ratios for a fatal or nonfatal cardiovascular event associated with the awake and asleep blood pressures, as derived at each step of data selection over 1000 bootstraps. After linearizing the horizontal axis by a logarithmic transformation, regression lines were fitted joining the data points from the recordings with 30 and 10 readings and from recordings including 20 and 7 readings during wakefulness and sleep, respectively. The last data points still on the regression line were derived from 8 readings during wakefulness and 4 during sleep. The number of daytime and nighttime readings required to predict a cardiovascular complication was 6 and 3, respectively.

## Discussion

Current guidelines [3–8] unanimously recommend ambulatory blood pressure monitoring as the state-of-the-art technology to be used to diagnose and manage hypertension. Current recommendations on the number of required readings focus on the management of hypertension in individual patients and vary from

obtaining at least 70% of the programmed readings without providing a specific number [6,9] to 20 awake or daytime and 7 asleep or nighttime readings [6]. However, in epidemiological or clinical studies, researchers often face the dilemma of applying these recommendations, thereby discarding potentially valuable information or accepting fewer readings to keep more recordings in the analyses. In reports of the IDACO database [10–12] or the Jackson Heart Study [23,24], the standard was set to 10 daytime and 5 nighttime readings. The novelty of the present analyses is that we demonstrated that in epidemiological studies 8 awake and 4 asleep or 6 daytime and 3 nighttime readings were sufficient to estimate the ambulatory blood pressure level, diagnose ambulatory hypertension and assess the relative risk of a cardiovascular complication.

Obviously, the higher the number of ambulatory readings obtained, the more representative a recording is for an individual's blood pressure level. However, cuff inflations during intermittent ambulatory blood pressure monitoring causes muscle compression, pain or discomfort at the arm [25–27], disturbs sleep [6,28–30], and therefore potentially affects the accuracy of blood pressure assessment [29,30], especially in hypertensive patients [27] or patients with sleeping disorders [29]. Cuff inflations can be extremely annoying in shift workers during the transition periods from daytime to nighttime work or in assembly-line workers, who have to keep up with an imposed production rhythm. In a recent study of 336 shift laborers doing chain work, we had to exclude 80 (23.8%) participants, because they declined ambulatory blood pressure monitoring ($n = 24$) or because they had fewer than 7 or 3 readings during wakefulness or sleep ($n = 56$) [31]. The discomfort caused by too frequent cuff inflation can also result in resistance from patients to having repeat ambulatory blood pressure monitoring [6]. These considerations explain why in clinical and epidemiological research, investigators have to strike a compromise between what might be ideal and what is acceptable to study participants. Based on our present findings, we do not suggest reducing the ambulatory blood pressure readings to

**Table 2.** Number of readings required for a 5% precision of the blood pressure differences in individual subjects.

| | Systolic/diastolic blood pressure thresholds | | | |
|---|---|---|---|---|
| N° of readings | Awake | Asleep | Daytime | Nighttime |
| 1 | 28.9 / 20.4 | 20.4 / 15.3 | 28.7 / 19.9 | 20.3 / 15.3 |
| 2 | 20.1 / 14.3 | 14.0 / 10.5 | 19.9 / 13.9 | 13.7 / 10.4 |
| 3 | 16.3 / 11.5 | 11.0 / 8.2 | 16.1 / 11.2 | 10.6 / 8.0 |
| 4 | 14.0 / 9.9 | 9.1 / 6.8 | 13.7 / 9.5 | 8.6 / 6.5 |
| 5 | 12.4 / 8.8 | 7.8 / 5.8 | 12.1 / 8.4 | 7.2 / 5.4 |
| 6 | 11.2 / 7.9 | 6.7 / 5.0 | 10.9 / 7.5 | 6.1 / 4.5 |
| 7 | 10.3 / 7.2 | 5.8 / 4.4 | 9.9 / 6.8 | 5.1 / 3.8 |
| 8 | 9.5 / 6.7 | 5.1 / 3.8 | 9.1 / 6.3 | |
| 9 | 8.9 / 6.2 | 4.4 / 3.4 | 8.4 / 5.8 | |
| 10 | 8.3 / 5.8 | 3.9 / 2.9 | 7.8 / 5.4 | |
| 11 | 7.8 / 5.5 | | 7.3 / 5.0 | |
| 12 | 7.4 / 5.2 | | 6.8 / 4.7 | |
| 13 | 7.0 / 4.9 | | 6.4 / 4.4 | |
| 14 | 6.7 / 4.7 | | 6.0 / 4.1 | |
| 15 | 6.4 / 4.5 | | 5.7 / 3.9 | |
| 16 | 6.1 / 4.3 | | 5.4 / 3.7 | |
| 17 | 5.8 / 4.1 | | 5.1 / 3.5 | |
| 18 | 5.6 / 3.9 | | 4.8 / 3.3 | |
| 19 | 5.4 / 3.8 | | 4.5 / 3.1 | |
| 20 | 5.1 / 3.6 | | 4.3 / 2.9 | |
| 21 | 4.9 / 3.5 | | | |
| 22 | 4.8 / 3.3 | | | |
| 23 | 4.6 / 3.2 | | | |
| 24 | 4.4 / 3.1 | | | |
| 25 | 4.3 / 3.0 | | | |
| 26 | 4.1 / 2.9 | | | |
| 27 | 4.0 / 2.8 | | | |
| 28 | 3.8 / 2.7 | | | |
| 29 | 3.7 / 2.6 | | | |
| 30 | 3.6 / 2.5 | | | |

A 5% precision indicates an absolute difference in the blood pressure level between reduced and full recordings within 2.5 to 97.5th percentile interval of the signed differences.

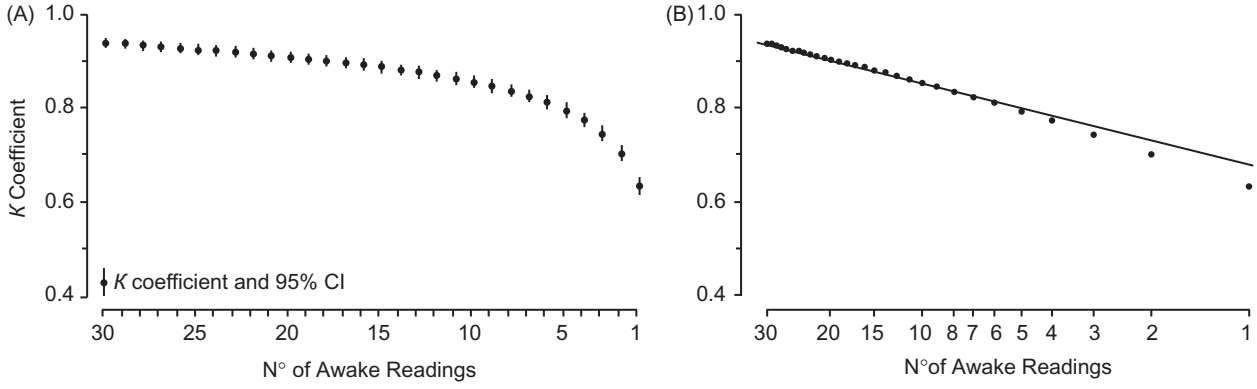


**Figure 3.** Concordance in the discrimination between normotension and hypertension during wakefulness. The κ statistic (A) was plotted for over 1000 bootstraps randomly reduced recordings. Vertical bars denote the 95% confidence interval. After linearizing the horizontal axis by a logarithmic transformation (B), regression lines were fitted joining the data points from recordings with 30 readings up to recordings including 20 readings. The last data point still on the regression line was 5 readings.

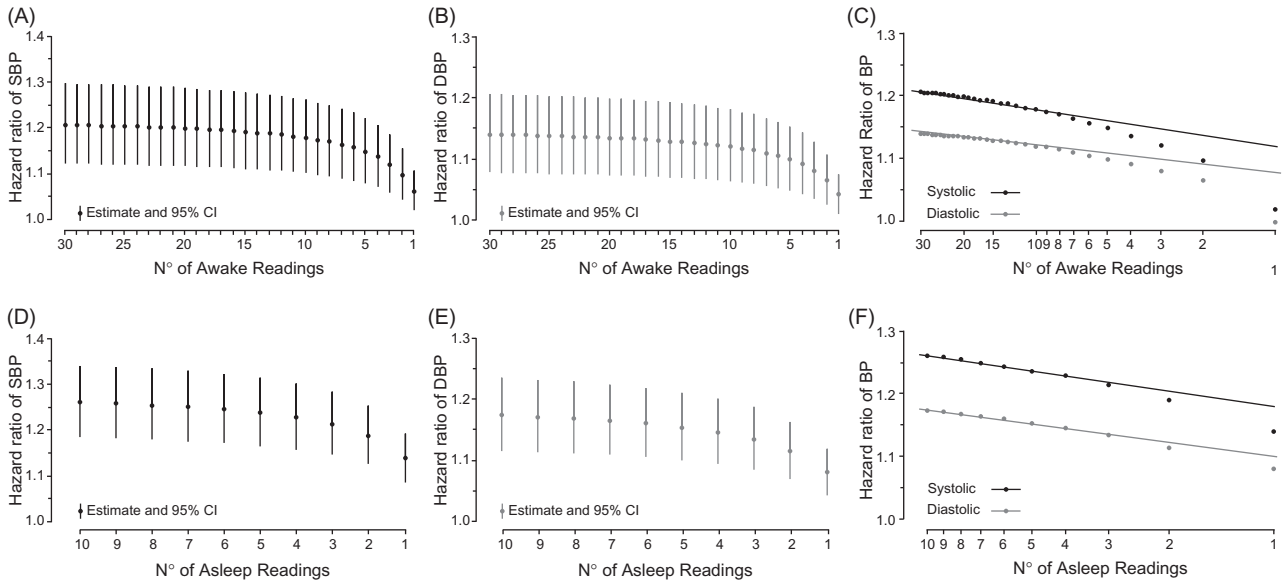


**Figure 4.** Multivariable-adjusted hazard ratios for a fatal or nonfatal cardiovascular complication associated with a 10-mm Hg higher systolic blood pressure (A,D [SBP]) or a 5-mm Hg higher diastolic blood pressure (B,E [DBP]) as derived from over 1000 bootstraps randomly reduced recordings during wakefulness (A,B) and sleep (D,E). Vertical bars denote the 95% confidence interval. After linearizing the horizontal axis by a logarithmic transformation, regression lines were fitted joining the data points from recordings including 30 to 20 readings during wakefulness (C) and from 10 to 7 readings during sleep (F). The last data points still on the regression line were derived from 8 readings during wakefulness and 4 during sleep.

less than what is common practice today in most studies. However, our observations suggest that in studies, in which the blood pressure level is the primary variable of interest, one might relax the guideline-endorsed criteria about the number of readings required to keep a maximum of study participants in the analysis.

More than 30 years ago, Di Rienzo and colleagues [32] addressed a similar research question in 40 hospitalized patients who underwent continuous intra-arterial blood pressure monitoring, using the Oxford method [33]. The intra-arterial blood pressure signal was analyzed by a computer to obtain the 24-h average blood pressure. The overall 24-h average was then compared with the average beat-to-beat blood pressure obtained by beat-to-beat analysis of periods ranging in duration from 30 minutes up to 12 hours. Differences between the 24-h and sub-period means remained prominent up to 4-h periods and only attenuated when blood pressure was averaged over 8 to 12 hours [32].

Our current findings combined with other studies highlighting the discomfort caused by cuff inflation raise the question whether cuffless blood pressure measurement might be an alternative to the oscillometric approach. Measurement of pulse transmit time is one approach to cuffless blood pressure monitoring. Pulse transit time is the interval between the peak of electrocardiographic R-wave and the arrival of the pulse wave in the fingertip or wrist as assessed by photoplethysmography [34]. However, cuffless measurements differed as much as -19.3 to 18.2 mm Hg from simultaneous oscillometric readings and the proportion of people with systolic blood pressure differences between the two methods exceeding 5 mm Hg was 45.9% and 65.7% in the supine and standing position, respectively [34]. For a smartphone-based application, the proportion of systolic readings deviating more than 5 mm Hg was 76.0% [35]. None of these devices would have passed current validation criteria for blood-pressure measuring devices [36].

Computation of blood pressure variability obviously requires more ambulatory readings than is required for the determination of blood pressure level. A previous IDACO publication had as objective to determine the minimum number of readings needed to compute average real variability (AVR) without loss of prognostic information [37]. ARV was first calculated from a discovery dataset that included 24-h ambulatory blood pressure measurements from 1254 residents (43.5% women; mean age, 56.6 years) of Copenhagen, Denmark. Concordance between ARV from full (80 or more blood pressure readings) and randomly reduced 24-h blood pressure recordings was examined, as was prognostic accuracy. A test dataset that included 5353 individuals (45.6% women; mean age, 54.0 years) with at least 48 blood pressure measurements from 11 randomly recruited population

cohorts was used to validate the results. In the test dataset, over 10.2 years (median), 806 participants died (335 cardiovascular including 206 cardiac deaths) and 696 experienced a major fatal or nonfatal cardiovascular event. Forty-eight blood pressure readings over 24 hours were adequate to compute ARV without meaningful loss of prognostic information [37].

The current study should be interpreted within the context of its limitations. First, our findings should not be used to reduce the number of programmed ambulatory blood pressure readings or lengthen the interval between ambulatory readings in managing individual patients in clinical practice. Clinicians should follow current guidelines [6,9] and obtain the maximum number of readings achievable within their health care setting and acceptable to their patients. However, Table 2 provides information of the number of ambulatory readings to estimate the blood pressure level with 5% precision in individual patients. It allows clinicians to determine the number of readings required for clinical research and patient management or choose for the same precision in both settings. Second, the number of required readings in our current analyses should not be extrapolated to studies with a focus on blood pressure variability or on the diurnal rhythmicity of blood pressure. However, compared with blood pressure level, blood pressure variability is a substantially weaker predictor of cardiovascular risk [37–39]. Third, for sake of generalizability, we reported the minimum number of daytime and night-time readings for investigators applying short fixed time intervals excluding the transition periods in the morning and evening when blood pressure usually changes rapidly [22]. However, the diary method to document wakefulness and sleep remains the approach to be favored [3–8]. Fourth, we simulated incomplete ambulatory blood pressure recordings by randomly removing readings from the full recordings. This procedure implicitly assumes that failed readings are missing at random. This assumption might not be true because measurement failure might occur more frequently during certain parts of the day as a consequence of noise due to physical activity or other stressors [40]. In addition, incomplete recordings might occur as a result of a subject taking off the recorder because of discomfort. However, the concern that readings might be missing not randomly would particularly apply to full 24 h ambulatory recordings, but to a lesser extent to separate analyses of the awake and asleep blood pressures or the day- and night-time blood pressures. Finally, we did not plot our results over a full 24-h recording period, because the variable number of recordings during wakefulness and sleep added too much complexity to the computations. However, compared with hypertension cross-classification by using 24-h ambulatory blood pressure derived from full readings, the κ statistic of randomly reduced recording were as high as 0.87 (CI, 0.86 to 0.88) if 8 awake and 4 asleep readings retained in current study.

In conclusion, in an epidemiological context, as few as 8 awake and 4 asleep or 6 daytime and 3 night-time readings are sufficient to estimate the ambulatory blood pressure level without meaningful loss of information in hypertension categorization or risk stratification. Experts might translate our observations into recommendations on the number of ambulatory readings to be included in analyses of clinical studies. To minimize discomfort for patients, guidelines should not only address the minimum number of readings to be obtained in patients during wakefulness and sleep, but also propose a threshold for the maximum number of readings that patients can tolerate without discomfort.

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## Disclosure statement

None of the authors declares a conflict of interest.

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